

**Table S6.** Nine highly conserved- or invariant- amino acid residues are present in shark A0 and are in close proximity to potentially interact with ligand in our A0 homology model.

| <b>A0</b> | <b>A2a</b> | <b>A1</b> | <b>reference</b>              |
|-----------|------------|-----------|-------------------------------|
| T112      | T88        | T91       | (Jiang, et al. 1996)          |
| F179      | F168       | F171      | (Lane, et al. 2012)           |
| D180      | E169       | E172      | (Kim, et al. 1996)            |
| N192      | N181       | N184      | (Lebon, et al. 2011)          |
| W260      | W246       | W247      | (Lane, et al. 2012)           |
| H264      | H250       | H251      | (Jiang, et al. 1997)          |
| N267      | N253       | N254      | (Lane, et al. 2012)           |
| S290      | S277       | T277      | (Lane, et al. 2012)           |
| H291      | H278       | H278      | (Askalan and Richardson 1994) |